

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

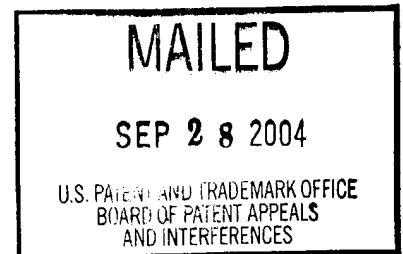
UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte XUANCHUAN YU and C. ALEXANDER TURNER JR.

Appeal No. 2004-1761
Application No. 10/044,807

ON BRIEF



Before WILLIAM F. SMITH, SCHEINER, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-4, all of the claims in the application. Claims 1 and 2 are representative and read as follows:

1. An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1.
2. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes amino acid sequence shown in SEQ ID NO: 2.

The examiner does not rely on any references.

Claims 1-4 stand rejected under 35 U.S.C. §§ 101 and 112, first paragraph, as lacking patentable utility.

We affirm.

Background

The specification discloses a "human polynucleotide encoding a protein sharing sequence similarity with mammalian proteases." Page 1. The "novel human protein (NHP) . . . shares sequence similarity with animal proteases, and particularly matrix metalloproteases, zinc dependent metalloproteases, and collagenases." Page 2.

More particularly, the specification discloses that "[t]he sequence data indicate that the NHP displays thrombospondin and disintegrin domains, and particular structural similarity to the ADAMTS family of metalloproteases. The NHP also displays similarity to receptor-linked phosphatases and membrane associated cell adhesion proteins." Pages 17-18. The gene encoding the NHP is apparently present on either chromosome 9 (page 3, lines 8-10) or chromosome 12 (page 18, lines 1-2).

The specification does not disclose what role the putative protease plays in any physiological process, but contemplates "processes for identifying compounds that modulate, i.e., act as agonists or antagonists, of NHP expression and/or NHP activity that utilize purified preparations of the described NHP and/or NHP product, or cells expressing the same. Such compounds can be used as therapeutic agents for the treatment of a wide variety of symptoms associated with biological disorders or imbalances." Page 3.

The specification also discloses that the gene corresponding to SEQ ID NO:1 has a total of seven polymorphic positions. See page 18. Presumably based on these polymorphisms, the specification discloses that

the present sequences can be used in restriction fragment length polymorphism (RFLP) analysis to identify specific individuals. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identification (as generally described in U.S. Patent No. 5,272,057, incorporated herein by reference). In addition, the sequences of the present invention can be used to provide polynucleotide reagents, e.g. PCR primers, targeted to specific loci in the human genome, which can enhance the reliability of DNA-based forensic identifications by, for example, providing another "identification marker" (i.e., another DNA sequence that is unique to a particular individual). Actual base sequence information can be used for identification as an accurate alternative to patterns formed by restriction enzyme generated fragments.

Page 12.

The specification discloses that "[t]he NHP proteins or peptides, NHP fusion proteins, NHP nucleotide sequences, host cell expression systems, antibodies, antagonists, agonists and genetically engineered cells and animals can be used for screening for drugs . . . effective in the treatment of the symptomatic or phenotypic manifestations of perturbing the normal function of a NHP in the body." Page 16. Or "the NHP products can be used as therapeutics. For example, soluble derivatives such as NHP peptides/domains corresponding to a NHP, . . . NHP antibodies . . . , antagonists or agonists . . . can be used to directly treat diseases or disorders." Pages 16-17.

The NHP protein is disclosed to have "a variety of uses. These uses include, but are not limited to, the generation of antibodies, as reagents in diagnostic assays, for the identification of other cellular gene products related to the NHP, and as reagents in assays for screening for compounds that can be used as pharmaceutical reagents

useful in the therapeutic treatment of mental, biological, or medical disorders and disease." Page 21.

The specification discloses that NHP-binding antibodies "may be used, for example, in the detection of a NHP in a biological sample and may, therefore, be utilized as part of a diagnostic or prognostic technique whereby patients may be tested for abnormal amounts of a NHP. . . . Such antibodies may additionally be used in methods for the inhibition of abnormal NHP activity. Thus, such antibodies may be utilized as a part of treatment methods." Pages 29-30.

Discussion

The examiner rejected all of the claims as lacking a disclosed utility sufficient to satisfy 35 U.S.C. § 101.¹ The examiner bears the initial burden of showing that a claimed invention lacks patentable utility. See In re Brana, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) ("Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility.").

The seminal decision interpreting the utility requirement of § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). At issue in Brenner was a claim to "a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced." Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on

¹ The examiner also rejected all of the claims under 35 U.S.C. § 112, first paragraph, for lack of enablement, but that rejection is merely as a corollary of the finding of lack of utility. See the Examiner's

the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that “where a claimed process produces a known product it is not necessary to show utility for the product.” Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be “useful,” that “simple, everyday word can be pregnant with ambiguity when applied to the facts of life.” Id. at 529, 148 USPQ at 693. Thus,

[it] is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the “new and useful” phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man’s grasp and where little or nothing is wholly beyond the pale of “utility”—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.²

The Court, finding “no specific assistance in the legislative materials underlying § 101,” based its analysis on “the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other.” Id. at 532, 148 USPQ at 695. The Court concluded that “[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—

Answer, pages 8-9. Therefore, our conclusion with respect to the § 101 issue also applies to the § 112 issue.

² The invention at issue in Brenner was a process, but the Court expressly noted that its holding “would apply equally to the patenting of the product produced by the process.” Id. at 535, 148 USPQ at 695-96.

there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.” Id. at 534-35, 148 USPQ at 695.

The Court considered and rejected the applicant’s argument that attenuating the requirement of utility “would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge.” The Court noted that, while there is value to encouraging disclosure, “a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development.” Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not “mean to disparage the importance of contributions to the fund of scientific information short of the invention of something ‘useful,’” and that it was not “blind to the prospect that what now seems without ‘use’ may tomorrow command the grateful attention of the public.” Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because “a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.” Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101’s utility

requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value “in the furtherance of steroid research and in the application of steroid materials to veterinary or medical practice.” Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly “show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests.” Id. at 939, 153 USPQ at 51.

The court held that “nebulous expressions [like] ‘biological activity’ or ‘biological properties’” did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants’ affidavit help their case: “the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know ‘how to use’ the compounds to find out in the first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are.” Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. “There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of ‘useful in research’ or ‘useful as building blocks of value to the researcher’ was recognized, and clearly rejected, by the Supreme Court” in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. “In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was ‘plastic-like.’” Id. at 1203, 26 USPQ2d at 1605. “Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility.” Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. See id., 26 USPQ2d at 1606. “[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there.” Id., 26 USPQ2d at 1605.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were “well recognized in the art as valuable for use in cancer chemotherapy.” Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court

noted that the data derived from the mouse model were “relevant to the treatment of humans and [were] not to be disregarded,” id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that “[it] is axiomatic that an invention cannot be considered ‘useful,’ in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious.” Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court “perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question.” Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by “marshal[ling] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds . . . , analogous to the benefit provided by the showing of an in vivo utility.” Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to

have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The claimed compounds were disclosed to have higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051,

224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best . . . on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

In this case, the examiner noted that the specification teaches that the protein encoded by the claimed polynucleotides shares sequence similarity to a variety of known proteins, including matrix metalloproteases, zinc-dependent metalloproteases, collagenases, receptor linked phosphatases, and membrane-associated cell adhesion proteins. Examiner's Answer, page 5. "However, the specification fails to identify any specific protein, with any specific and substantial function, to which the instant protein, as set forth by SEQ ID NO:2, is homologous." Id. According to the examiner's sequence comparisons, "[s]equence searches showed no consistent homology for the full-length SEQ ID NO:2 with metalloproteases." Id. The examiner cited three PCT patent applications as disclosing sequences having high degrees of homology with SEQ ID NO:2 but no disclosed function. See id., page 5-6. The examiner concluded that "a

specific and substantial or well-established utility for the polypeptide of SEQ ID NO:2 cannot be deduced based on homology to known proteins." Id., page 6.

Appellants argue that the protein encoded by the claimed nucleic acids would be accepted as a protease by those skilled in the art, because

two sequences sharing nearly 100% identity at the protein level over an extended region of the claimed sequence are present in the leading scientific repository for biological sequence data (GenBank), and have been annotated by third party scientists wholly unaffiliated with Appellants as "Homo sapiens ADAMTS-like 1" variants 1 and 2. . . . [T]here can be no question that those skilled in the art would clearly believe that Appellants' sequence is an ADAMTS-like protease, and would thus readily understand the utility of the presently claimed sequence.

Appeal Brief, page 13.

We do not agree that the similarity of the protein encoded by the claimed nucleic acids to known proteins establishes its utility. As the examiner pointed out, the specification discloses that the encoded protein share sequence similarity with a variety of proteins, having varied biological functions and activities. Granted, most of the similar proteins are proteases, but the specification admits that proteases are involved in a variety of diverse biological functions (see page 1, lines 25-31) and no specific function is disclosed for the encoded protein.

We do not find that Appellants' comparison with the GenBank sequence of an ADAMTS-like protein establishes the function or utility of the protein encoded by the claimed polynucleotides. First, Appellants have provided no sequence comparison showing exactly how the two protein sequences compare; thus, we have nothing but Appellants' characterization to show that the sequences are "nearly 100%" identical "over an extended region." Even assuming Appellants' characterization is objectively

accurate, however, that sequence similarity would not suffice to establish the function or activity of the encoded protein. The longest of the GenBank sequences is only 683 amino acids long, while SEQ ID NO:2 is 1762 amino acids long (specification, page 2, lines 10-12. Thus, the protein encoded by the claimed polynucleotides is more than twice as long as the GenBank sequence; no explanation has been provided regarding the effect of the uncharacterized 60% of the encoded protein on its activity.

Finally, even assuming that the protein encoded by the claimed polynucleotides is accurately characterized as an ADAMTS-like metalloprotease, neither the specification nor any evidence of record discloses any utility that would be implied by such a characterization. The evidence of record does not disclose the role of such proteases in any biological process, or the proteins that are cleaved by such proteases, or the effect that proteolytic cleavage has on the substrate protein(s) (e.g., activation of a proenzyme or degradation of the substrate). For all these reasons, we agree with the examiner that the claimed polynucleotides are not supported by a patentable utility based on the activity of the encoded protein.

Appellants also argue that the claimed polynucleotides are useful because of the disclosed polymorphisms in SEQ ID NO:1: "As such polymorphisms are the basis for forensic analysis, which i[s] undoubtedly a 'real world' utility, the presently claimed sequence must in itself be useful." Appeal Brief, page 4. "The fact that forensic biologists use polymorphic markers such as those described by Appellants every day provides more than ample support for the assertion that forensic biologists would also be able to use the specific polymorphic markers described by Appellants in the same fashion." Id., page 5.

This argument is not persuasive. As their basis for asserting that the disclosed polymorphisms provide utility for the claimed polynucleotides, Appellants cite to "the specification as originally filed, at least page 3, line 15, and from page 11, line 31 to page 12, line 27." Appeal Brief, page 4.

We do not find support for the asserted utility in the cited passages. The sentence on page 3 that includes line 15 reads as follows: "The sequences of the present invention are also useful as additional DNA markers for restriction fragment length polymorphism (RFLP) analysis, and in forensic biology." Page 11, line 31, to page 12, line 27 reads as follows:

The identification and characterization of human genomic clones is helpful for identifying polymorphisms (including but not limited to, nucleotide repeats, microsatellite alleles, single nucleotide polymorphisms, or coding single nucleotide polymorphisms), determining the genomic structure of a given locus/allele, and designing diagnostic tests. For example, sequences derived from regions adjacent to the intron/exon boundaries of the human gene can be used to design primers for use in amplification assays to detect mutations within the exons, introns, splice sites (e.g., splice acceptor and/or donor sites), etc., that can be used in diagnostic and pharmacogenomics.

For example, the present sequences can be used in restriction fragment length polymorphism (RFLP) analysis to identify specific individuals. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identification (as generally described in U.S. Patent No. 5,272,057, incorporated herein by reference). In addition, the sequences of the present invention can be used to provide polynucleotide reagents, e.g. PCR primers, targeted to specific loci in the human genome, which can enhance the reliability of DNA-based forensic identifications by, for example, providing another "identification marker" (i.e., another DNA sequence that is unique to a particular individual). Actual base sequence information can be used for identification as an accurate alternative to patterns formed by restriction enzyme generated fragments.

Having reviewed the cited parts of the specification, we find no clear teaching of how the disclosed polymorphisms would be used by those skilled in the art in, e.g., forensic analysis. The specification asserts that the claimed sequences can be used in RFLP analysis; i.e., a technique in which “an individual’s genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identification.” However, the specification does not disclose that the presence of different nucleotides at any of the seven polymorphic positions in SEQ ID NO:1 in fact results in “unique bands” in different individuals.

The specification incorporates by reference U.S. Patent 5,272,057 for its description of RFLP analysis. We have reviewed the cited patent, but do not find in its discussion of RFLP analysis a basis for imputing utility to the presently claimed polynucleotides. The ‘057 patent describes RFLP as follows:

Restriction Fragment Length Polymorphism (RFLP). The genomic DNA of two individuals in a population will differ in sequence at many sites either as a result of change in bases or insertions or deletions of sequences. When these differences occur in the recognition site for a restriction endonuclease, then a polymorphism in the length of restriction fragments produced by digestion of the DNA of the two individuals will result.

Column 3, lines 53-61 (emphasis added).

Here, there is no evidence of record showing that any of the seven polymorphisms disclosed to exist in SEQ ID NO:1 occur in the recognition site of a restriction endonuclease, as required in order for them to be useful in RFLP analysis. Appellants have not pointed to any specific restriction enzyme that cuts or fails to cut at a specific position in SEQ ID NO:1 depending on the presence or absence of a specific

polymorphism. Thus, the evidence of record does not support the asserted utility of SEQ ID NO:1 in RFLP analysis.

The specification also discloses that “base sequence information can be used for identification as an accurate alternative to patterns formed by restriction enzyme generated fragments,” page 12, but we do not find that this disclosure satisfies § 101. First, the specification provides no further explanation of how the use of “base sequence information” provides a patentable utility for the claimed “nucleic acid molecule[s].” That is, while the presence of a restriction fragment length polymorphism may imply a utility for nucleic acid molecules containing the RFLP site (since the nucleic acid molecule could be labeled and used as a hybridization probe), the same is not true for a polymorphism that must be identified by DNA sequencing: if the presence of a polymorphism must be identified by sequencing, then any polymorphism-based methods do not involve using the claimed nucleic acids but instead only involve sequencing the subject’s DNA. Appellants have not adequately explained how such a method makes the claimed product “useful”, as required by § 101, when the claimed product is not even used in the method.

In addition, utility must be commensurate in scope with the claims. See In re Langer, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA 1974): “[A] specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is reason for one skilled in the art to question the objective truth of the statement of utility or its scope” (first emphasis added). Here, the use of the seven polymorphic positions in SEQ ID NO:1 in forensic

analysis at best provides some utility for those seven bases in SEQ ID NO:1. The claims, however, are directed not just to the full-length, 5289-nucleotide nucleic acid molecule of SEQ ID NO:1, but also to all other nucleic acid molecules that encode the same amino acid sequence (SEQ ID NO:2). The claimed nucleic acid molecules need not have either of the bases that naturally occur at the seven polymorphic positions. For example, the specification discloses that position 2613 of SEQ ID NO:1 can be either A or C, both of which give an isoleucine (Ile) at position 871 of SEQ ID NO:2. Page 18, lines 10-13. However, a T at the same position of SEQ ID NO:1 would also give isoleucine at amino acid 871 of SEQ ID NO:2.³ At each of the other six polymorphic positions as well, the amino acid sequence of SEQ ID NO:2 would result from nucleic acid sequences containing neither of the naturally occurring bases. Even assuming arguendo, therefore, that the polymorphisms in SEQ ID NO:1 are useful, that usefulness is in no way commensurate with the scope of the claims, including and especially claim 2.

Finally, Appellants have provided no evidence to show that those skilled in the art would have found the specific polymorphisms present in SEQ ID NO:1 – without analysis of their degree of variability in the human population and without associating them with any other genetic marker – to be useful as argued. Thus, the evidence of record does not support the polymorphism-based utilities asserted in the Appeal Brief; those asserted utilities do not overcome the rejection.

³ According to the genetic code, of which we take judicial notice, the codons ATC, ATA, and ATT all code for isoleucine. The codon in SEQ ID NO:1 made up of nucleotides 2611 to 2613 is ATC; according to the specification, these bases read ATA in some individuals and still code for isoleucine. Claim 2 reads on a non-naturally occurring sequence having the codon ATT and also encoding isoleucine.

Appellants also argue that the claimed nucleic acids are useful in "gene chip" methods of tracking gene expression, and that "[e]xpression profiling does not require a knowledge of the function of the particular nucleic acid on the chip." Appeal Brief, page 12. See also page 11:

Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents. . . . Clearly, compositions that enhance the utility of such DNA gene chips, such as the presently claimed nucleotide sequences, must in themselves be useful.

Appellants argue that, in addition to their use in "DNA chips", the claimed sequences also have "utility in mapping the protein encoding regions of the corresponding human chromosome, specifically chromosome 9." Id., page 10.

Appellants also argue that

[t]he presently claimed polynucleotide sequence provides biologically validated empirical data (e.g., showing which sequences are transcribed, spliced, and polyadenylated) that specifically defines that portion of the corresponding genomic locus that actually encodes exon sequence.

Id., pages 10-11. Appellants argue that "the described sequences are useful for functionally defining exon splice-junctions," id., page 11, and that "the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts." Id., page 10.

We are not persuaded by Appellants' argument. We find that these asserted uses of the claimed polynucleotides—as a component of a DNA chip for monitoring gene expression, as a marker for a given chromosomal locus, or for defining the exon splice-junctions of a gene—do not satisfy the utility requirement of § 101. Such uses do not provide a specific benefit in currently available form.

For example, with regard to the asserted “DNA chip” utility, we accept for argument’s sake that a person skilled in the art could attach one of the claimed polynucleotides (or a part of it) to a solid substrate, in combination with other polynucleotides, to form a DNA chip, and that such a DNA chip could be used to monitor changes in expression of the corresponding gene. However, the specification provides no guidance to allow a skilled artisan to use data relating to the expression of the gene comprising SEQ ID NO:1 in any practical way. The specification provides no guidance regarding what the SEQ ID NO:1-specific information derived from a DNA chip would mean.

For example, assume that a fragment of SEQ ID NO:1 was attached to a DNA chip and the researcher observed that expression of the corresponding gene was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to determine what, if anything, that result means. Perhaps a change in expression of the gene would mean different things, depending on other factors, but again the specification provides no hint what other factors might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), or the degree of increase? Because the specification does not disclose the activity of the protein encoded by SEQ ID NO:1, it provides no guidance as to how to interpret the results of a DNA chip-based gene expression assay based on the claimed polynucleotides.

The same problem afflicts Appellants’ assertions that the claimed polynucleotides can be used to map a particular chromosomal locus or to define the exon splice-

junctions of the genomic gene: the specification provides no meaningful guidance regarding how to use such information in any practical way. What would it mean, for example, if SEQ ID NO:1 hybridizes to a specific part of human chromosome 9, or if SEQ ID NO:1 can be used to show that the chromosomal gene has an exon splice junction between nucleotides 103 and 104? The specification provides no guidance on how such information would allow those skilled in the art to use the claimed polynucleotides in a specific, substantial way. By contrast, if the specification disclosed, for example, that SEQ ID NO:1 hybridized adjacent to a chromosomal locus associated with a known disease (e.g., a locus susceptible to a cancer-causing translocation), the sequence would have an apparent utility in disease diagnosis. However, without disclosure of a specific use for the resulting data, using the claimed sequences for mapping or determining exon splice-junctions amounts to research on the claimed polynucleotides themselves.

In effect, Appellants' position is that the claimed polynucleotides are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. We do not agree that such a disclosure provides a "specific benefit in currently available form." Rather, the instant case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, Appellants claim a product asserted to be useful in a method of generating gene-expression or gene-mapping data, but the specification does not disclose how to interpret those data. Just as the process claimed

in Brenner lacked utility because the specification did not disclose how to use the end-product, the product claims here lack utility, based on their use in, e.g., DNA chips, because the specification does not disclose how to use the SEQ ID NO:1-specific gene expression data generated by a DNA chip.

Appellants argue that the claimed polynucleotides could potentially be part of a DNA chip; since DNA chips have utility, compounds that “enhance the utility of such DNA chips, such as the presently claimed nucleotide sequence, must in themselves be useful.” Appeal Brief, page 11. We disagree.

Assuming arguendo that a generic DNA chip—one comprising a collection of uncharacterized or semi-characterized gene fragments—would provide a useful tool for, e.g., drug discovery, it does not follow that each one of the polynucleotides represented in the DNA chip individually has patentable utility. Although each polynucleotide in the DNA chip contributes to the data generated by the DNA chip overall, the contribution of a single polynucleotide—its data point—is only a tiny contribution to the overall picture.

The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a DNA chip, for example, does not necessarily mean that every one of the components of the DNA chip also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101’s utility requirement in order to be patentable; it must provide a specific benefit in currently available form. Providing a single data point among thousands, even if the thousands of data points collectively are useful, does not meet this standard.

The Supreme Court noted that the patent system contemplates a basic quid pro quo: in exchange for the legal right to exclude others from his invention for a period of time, an inventor discloses his invention to the public. See Brenner, 383 U.S. at 534, 148 USPQ at 695. The Brenner Court held that the grant of patent rights to an applicant is justified only by disclosure of an invention with substantial utility – a specific benefit in currently available form. Until the invention has been refined and developed to this point, the Court held, the applicant has not met his side of the bargain, and has not provided a disclosure that justifies granting him the right to exclude others. See id.

Thus, the basic quid pro quo of the patent system is the grant of a valuable legal right in exchange for a meaningful disclosure of the claimed invention. In this case, the generic utilities disclosed for the claimed products do not entitle Appellants to the legal right they claim to exclude others from using those products.

We note that this application is one of several on appeal that share the same assignee.⁴ In each of these cases, regardless of the specific facts of the case, the appellants have asserted the same DNA chip, gene-mapping, and exon splice junction arguments. It would therefore appear that Appellants view these potential uses as utilities that can be asserted for any cDNA they isolate, regardless of how little is known about it, which (they hope) will nonetheless serve as a basis for patent protection and secure for Appellants any value that might become apparent in the future, after they or others have further characterized the claimed products. This is precisely the type of result that the Brenner Court sought to avoid by requiring disclosure of a substantial

⁴ Such applications include 09/460,594 (Appeal No. 2003-1528), 09/804,969 (2003-1794); 09/802,116 (2003-2017); 09/822,807 (2003-2028); and 09/564,557 (2004-0343).

utility to satisfy § 101. See 148 U.S. at 535-36, 148 USPQ at 696: [The Court was not] “blind to the prospect that what now seems without ‘use’ may tomorrow command the grateful attention of the public. But a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.” Id.

The polynucleotides of the instant claims may indeed prove to be useful (and valuable), after the in vivo role of the encoded protein is discovered. The work required to confer value on the claimed products, however, remains to be done. The instant specification’s disclosure does not justify a grant of patent rights. See Brenner, 383 U.S. at 534, 148 USPQ at 695: “[A] process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development.” We consider the Brenner Court’s concern about the “power to block off whole areas of scientific development” to be equally applicable here.

Finally, adopting the per se rule that Appellants seek—that any expressed human gene has utility because it can be used in a DNA chip—would mean that almost any naturally occurring nucleic acid would be patentable. Appellants’ reasoning does not depend on the biological function of the protein encoded by the claimed nucleic acids, and so would apparently apply to any expressed human gene, as well as fragments of them (see, e.g., the specification at page 8, lines 24-32).

Nor can the rationale be confined to expressed human genes. We can take judicial notice of the fact that other organisms are of interest for many different reasons, such that gene expression assays could conceivably be used in their research. For example, some organisms are of interest to researchers because they have been historically well-studied (e.g., yeast and Arabidopsis). Others are of interest because they are used as animal models (e.g., mice and chimpanzees), because they are commercially valuable (e.g., pigs and tomatoes), because they are pests (e.g., ragweed and corn borers), or because they are pathogens (e.g., Candida and various bacteria). Under Appellants' proposed rule, hybridizable fragment of any gene of any of these organisms—and probably most other organisms—would be found to have patentable utility because it could be attached to a chip and used in "research" to see what happens to expression of that gene under various conditions.

Appellants' reasoning would also vitiate the enablement requirement, since "[t]he enablement requirement is met if the description enables any mode of making and using the invention." Johns Hopkins Univ. v. CellPro Inc., 152 F.3d 1342, 1361, 47 USPQ2d 1705, 1714 (Fed. Cir. 1998) (quoting Engel Indus., Inc. v. Lockformer Co., 946 F.2d 1528, 1533, 20 USPQ2d 1300, 1304 (Fed. Cir. 1991)). If we were to agree with Appellants that any expressed gene and any hybridizable fragment thereof is useful in a DNA chip, then we would also have to hold that the specification has taught those skilled in the art one mode of using the invention. Thus, Appellants' rule of per se utility would also require a corresponding rule of per se enablement.

Under Appellants' rule, then, any polynucleotide from an expressed gene would be patentable if it was adequately described in the specification and was not disclosed

or suggested in the prior art. This standard, however, is not the one set by Congress, which requires that a patentable invention also be useful and fully enabled, nor is it the standard that has been consistently applied by the courts.

In addition, the flood of DNA patents that would result from adoption of Appellants' rule could doom the potential contribution of microarrays to biological research. Appellants argue that "[g]iven the widespread utility of such 'gene chip' methods using public domain gene sequence information . . . , there can be little doubt that the use of the presently described novel sequences would have great utility in such DNA chip applications." Appeal Brief, page 12.

The practical effect of Appellants' utility standard, however, would be that making a microarray with 1000 genes represented on it would require investigating each of the DNA sequences (and subsequences) on the gene chip to ensure that it was not the subject of someone else's patent. For each of the DNAs that was the subject of someone else's patent claim, a license would have to be negotiated – potentially thousands of such negotiations for the finished product. These transaction costs would have to be incurred for each new product that an aspiring gene chip manufacturer wished to market. The industry gridlock likely to result has been termed a "tragedy of the anticommons:"

By conferring monopolies in discoveries, patents necessarily increase prices and restrict use—a cost society pays to motivate invention and disclosure. The tragedy of the anticommons refers to the more complex obstacles that arise when a user needs access to multiple patented inputs to create a single useful product. Each upstream patent allows its owner

to set up another tollbooth on the road to product development, adding to the cost and slowing the pace of downstream biomedical innovation.

Heller, page 698.⁵

The Supreme Court has warned against allowing too many "tollbooths" on the road to innovation:

Patents . . . are meant to encourage invention by rewarding the inventor with the right, limited to a term of years fixed by the patent, to exclude others from the use of his invention. . . . But in rewarding useful invention, the "rights and welfare of the community must be fairly dealt with and effectually guarded." Kendall v. Winsor, 21 How. 322, 329 (1859). . . . To begin with, a genuine "invention" or "discovery" must be demonstrated "lest in the constant demand for new appliances the heavy hand of tribute be laid on each slight technological advance in an art."

Sears, Roebuck & Co. v. Stiffel Co., 376 U.S. 225, 230, 140 USPQ 524, 527 (1964).

Summary

The basic quid pro quo of the patent system requires disclosure of an invention having substantial utility. Appellants' disclosure in this case does not provide a specific benefit in currently available form, and therefore lacks the substantial utility required by 35 U.S.C. § 101. We therefore affirm the rejections for lack of utility.

⁵ Heller et al., "Can patents deter innovation? The anticommons in biomedical research," Science, Vol. 280, pp. 698-701 (1998). Accessible online at www.sciencemag.org/cgi/content/full/280/5364/698.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

William F. Smith)
William F. Smith)
Administrative Patent Judge)

Toni R. Scheiner) BOARD OF PATENT
Toni R. Scheiner)
Administrative Patent Judge)

Eric Grimes) APPEALS AND
Eric Grimes)
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